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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/765,244	10/30/1997	PETER SEIBEL	8484-018-999	5827

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GREENLEE WINNER AND SULLIVAN P C
5370 MANHATTAN CIRCLE
SUITE 201
BOULDER, CO 80303

EXAMINER

LACOURCIERE, KAREN A

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 12/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/765,244

Applicant(s)

SEIBEL ET AL.

Examiner

Karen A. Lacourciere

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 84-134 is/are pending in the application.
- 4a) Of the above claim(s) 105-134 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 84-104 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the paper filed 09-23-2003 is acknowledged. The traversal is on the ground(s) that the search of the invention of both Group I and II would not be a burdensome search because the constructs only differ in structure in that the nucleic acid is linear versus cyclic. This is not found persuasive because the search for each of the inventions of Group I and II would be a separate and distinct search based on the difference in structure of these constructs and, therefore, would be an undue burden.

Applicant's election without traverse of SEQ ID NO:22 in the paper filed 09-23-2003 is acknowledged. The requirement is still deemed proper and is therefore made FINAL.

Claims 105-134 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the paper filed 09-23-2003.

Chimeric peptide nucleic acids constructs comprising SEQ ID NO:1 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the paper filed 09-23-2003.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Drawings

The substitute drawing for Figure 6B was received on 09-23-2003. This substitute drawing is acceptable.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 103 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 103 recites the limitation "derivative thereof". It is unclear what kinds of modifications and the degree of modifications could be made to a molecule and have that molecule be considered a "derivative" of MBS, rather than an entirely different molecule. The skilled artisan could not determine what linkage agents would or would

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not be encompassed in this term and therefore could not determine the scope of the claimed invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 92 and 93 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendments filed 03-14-2003 have added the limitations wherein the linkage group is bound to the nucleic acid via a spacer comprising at least two carbon atoms (claim 92) or comprising six carbon atoms (claim 93). Applicant has not pointed to any support for these newly added limitations and support for these limitations could not be found in the originally filed specification or claims. To overcome this rejection Applicant should direct the examiner to specific support for these limitations in the originally filed specification or claims or delete these limitations.

Claims 84-104 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

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one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 84-104 are drawn to peptide nucleic acid chimeras which comprise a broad genus of mitochondrial signal peptides, but the specification only discloses two members of the genus, SEQ ID NO:1 and SEQ ID NO:22, which are both signal peptides directed to the mitochondrial matrix isolated from rats. The specification does not appear to disclose any signal peptides for mitochondrial compartments other than the mitochondrial matrix, nor does the specification provide mitochondrial signal peptide sequences from any species other than the rat. There is no indication in the specification of how to identify or obtain other members of the claimed genus. Due to the variation in structure (ie amino acid sequence) among members of the claimed genus, one skilled in the art would not recognize that the applicant was in possession of the necessary common features and attributes of the claimed genus, because the two disclosed signal peptides (from the same species of organism) would not be representative of the claimed genus, which is highly variant.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 1 and SEQ ID NO:22, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides

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and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." *Id.* at 1170, 25 USPQ2d at 1606.

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not

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necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, only SEQ ID NO: 1 but not the full breadth of the claims meet the written description provision of 35 USC 112, first paragraph. The one species specifically disclosed (i.e. SEQ ID NO: 1) is not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 84-86, 89, 90, 92, rejected under 35 U.S.C. 102(b) as being anticipated by Vestweber et al. for the reasons of record set forth in the prior Office action (mailed 07-05-00). Applicants have not provided any arguments pertaining to the rejection of record.

Vestweber et al. teach a protein DNA conjugate wherein the c-terminal cysteine of the protein is linked to a DNA molecule via an aminoethyl linker group using a heterobifunctional linkage agent (maleimidobenzoyl-N-hydroxysuccinimide). The

protein portion comprises a mitochondrial signal peptide (specifically, yeast cytochrome oxidase subunit IV presequence) which has a reactive cysteine at the c-terminus. The nucleic acid portion is linked at the 5'-terminal hydroxyl group and comprises either a double stranded (which comprises two helical turns) or single stranded DNA 24-mer, which contains regions of complementarity so, therefore, the singlestranded DNA may form a hairpin and said hairpin would include overhanging ends as the ends are not complementary. The DNA is "partially palindromic", as it comprises the sequence "TAAT", which is a four base palindrome. The DNA conjugate is capable of overcoming the mitochondrial membrane by using natural transport mechanisms. Further, the disclosed DNA-protein conjugate is used in a method to deliver a nucleic acid into a mitochondria wherein the conjugate is mixed with pretreated energized mitochondria.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 25 and 37 are maintained as rejected under 35 U.S.C. 103(a) as being unpatentable over Vestweber et al. in view of Williams et al. further in view of Latham et

al. for the reasons of record set forth in the prior Office action (mailed 07-05-00).
Applicants have not provided any arguments pertaining to the rejection of record.

Conclusion

Any inquiry concerning this communication should be directed to Karen A. Lacourciere at telephone number (703) 308-7523.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached at (703) 308-0447. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Lacourciere

December 15, 2003


KAREN A. LACOURCIERE, Ph.D
PRIMARY EXAMINER